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ATTORNEY DOCKET NO. 10990105-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): CAREN, MICHAEL P.

Serial No.: 09/302,898

Examiner: FORMAN, BETTY J

Filing Date: April 30, 1999

Group Art Unit: 1634

Title: POLYNUCLEOTIDE ARRAY FABRICATION

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria VA 22313-1450

TRANSMITTAL OF APPEAL BRIEF

Sir:

Transmitted herewith is the Appeal Brief in this application with respect to the Notice of Appeal filed on April 24, 2006

The fee for filing this Appeal Brief is (37 CFR 1.17(c)) **$500.00**.

(complete (a) or (b) as applicable)

The proceedings herein are for a patent application and the provisions of 37 CFR 1.136(a) apply.

☐ (a) Applicant petitions for an extension of time under 37 CFR 1.136 (fees: 37 CFR 1.17(a)(1)-(5)) for the total number of months checked below:

☐	one month	$ 120.00
☐	two months	$ 450.00
☐	three months	$1020.00
☐	four months	$1590.00

☐ The extension fee has already been filled in this application.

☒ (b) Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

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APPELLANTS' BRIEF	Attorney Docket No.	10990105-1
	Confirmation No.	7610
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Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Filing Date	April 30, 1999
	Group Art Unit	1634
	Examiner Name	FORMAN, BETTY J.
	Title: "METHODS AND DEVICES FOR POLYNUCLEOTIDE ARRAY FABRICATION"	

Sir:

This Brief is filed in support of Appellants' appeal from the Examiner's Final Rejection dated December 23, 2005. No claims have been allowed, and Claims 1-18 and 20-48 are pending. Claims 1-18 and 20-48 are appealed. A Notice of Appeal was filed on April 24, 2006.

The Board of Appeals and Interferences has jurisdiction over this appeal pursuant to 35 U.S.C. §134.

The Commissioner is hereby authorized to charge deposit account number 50-1078, reference no. 10990105-1 to cover any fee required under 37 C.F.R. §1.17(c) for filing Appellants' brief. In the unlikely event that the fee transmittal or other papers are separated from this document and/or other fees or relief are required, Appellants petition for such relief, including extensions of time, and authorize the Commissioner to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to deposit account number 50-1078, reference no. 10990105-1.

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REAL PARTY IN INTEREST

The inventors named on this patent application assigned their entire rights in the invention to Agilent Technologies, Inc.

RELATED APPEALS AND INTERFERENCES

An appeal is pending in Application Serial No. 09/359,527 which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.

STATUS OF CLAIMS

The present application was filed on April 30, 1999 with Claims 1-40. During prosecution, Claim 41-48 were added and Claim 19 was cancelled. Accordingly, Claims 1-18 and 20-48 are pending in the present application, all of which claims are currently rejected and appealed herein.

STATUS OF AMENDMENTS

No amendments to the Claims were filed subsequent to issuance of the Final Rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

The present invention provides a method for fabricating an array of polynucleotides on a substrate. The method includes depositing an array of polynucleotide containing fluid droplets on the substrate to provide, when dry, a target pattern of polynucleotide containing dried spots. Any device or apparatus which can be used to deposit droplets in an array can be used as a deposition system to accomplish this. The target pattern is an aim or desired pattern. A sufficient time is allowed to pass such that droplets deposited by the system will have dried to yield an actual pattern of dried spots. The actual pattern is then

observed and compared with the target pattern.

Below is a description of each appealed claim. Where support for each claim can be found in the specification is listed in parentheses, is given as exemplary, and is not intended to be exhaustive.

Independent Claim 1 claims a method for fabricating an array of polynucleotides on a substrate. The method includes operating a deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate to provide, when dry, a target pattern of polynucleotide containing dried spots. The target pattern is an aim or desired pattern. A sufficient time is allowed to pass such that droplets deposited by the system will have dried to yield an actual pattern of dried spots. The actual pattern is then observed and compared with the target pattern. (See the specification, pg. 3, line 27 to page 4, line 6.)

Claim 2 depends from Claim 1 and specifies that the actual pattern is observed by capturing an image of the actual pattern (See the specification pg 4, lines 4 and 5.)

Claim 3 depends from Claim 1 and specifies that the system deposits fluid droplets at least some of which contain respective different polynucleotides (See the specification pg 4, lines 14 and 15.)

Claim 4 depends from Claim 1 and specifies that one or more polynucleotide containing fluids each comprise a solution of a polynucleotide and a sufficient amount of salt to enhance polynucleotide imaging. (See the specification pg 4, lines 16 and 17.)

Claim 5 depends from Claim 1 and specifies that the polynucleotides are DNA of at least six nucleotides in length. (See the specification pg 4, lines 21 and 22.)

Claim 6 depends from Claim 5 and specifies that the DNA is cDNA. (See the specification pg 4, line 23.)

Claim 7 depends from Claim 5 and specifies that the DNA is single stranded. (See the specification pg 4, line 24.)

Claim 8 depends from Claim 1 and specifies that the comparison includes a comparison of dried actual spot locations or dimensions with target locations or dimensions. (See the specification pg 4; lines 12 and13.)

Claim 9 depends from Claim 1 and specifies that the comparison includes a comparison of the presence or absence of dried spots at target locations. (See the specification pg 4; line 8.)

Claim 10 depends from Claim 1 and specifies that the image capture comprises imaging a light scattering characteristic of dried spots. (See the specification pg 4; lines 26 and 27.)

Claim 11 depends from Claim 1 and specifies that the image capture comprises imaging a fluorescence characteristic of dried spots. (See the specification pg 4, line 28.)

Claim 12 depends from Claim 1 and specifies that the method additionally comprises generating a signal indicative of the result of the comparison. (See the specification pg 18, lines 30 and 31.)

Claim 13 depends from Claim 1 and specifies that the deposition system is operated to fabricate multiple polynucleotide arrays on a same substrate. (See the specification pg 4, lines 29 and 30.)

Claim 14 depends from Claim 1 and specifies that the method additionally comprises storing an error indication in association with an array when the results of one or more comparisons for that array exceed a predetermined tolerance. (See the specification pg 4, line 32 to pg 5, line 1.)

Claim 15 depends from Claim 14 and specifies that the deposition system is operated to fabricate multiple polynucleotide arrays, the method additionally comprising rejecting the array associated with a stored error indication. (See the specification pg 4, line 30.)

Claim 16 depends from Claim 14 and specifies that the error indication is stored in a memory, the method additionally comprising writing on a medium an identification for the array associated with an error indication; physically associating that medium with the array; and storing the identification in the memory. (See the specification pg 5, line 12.)

Claim 17 depends from Claim 16 and specifies that the error indication includes an indication of the magnitude of the error. (See the specification pg 5, line 3.)

Independent Claim 18 claims a method of fabricating an array of polynucleotides on a substrate, comprising operating a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system which may differ from the actual pattern deposited; capturing an image of the actual pattern; comparing the actual pattern with the target pattern; when the results of one or more comparisons for an array identify the presence of a first level error, generating a first level error indication associated with the array; writing the error indication or an identification of the error indication, on a medium; physically associating the medium with the array; and, when an identification of the error indication is written on the medium, storing the identification in a memory in association with the error indication; and forwarding the array and medium to a remote user. (See the specification pg 5, lines 6-8.)

Claim 20 depends from Claim 1 and specifies that the polynucleotide deposition system automatically fabricates multiple polynucleotide arrays, the method additionally comprising, when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, automatically halting further operation of the deposition system and generating a visible or audible operator alert. (See the specification pg 5, lines 17 and 18.)

Claim 21 depends from Claim 1 and specifies that the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and the method additionally comprises generating an error indication when the results of one or more comparisons for an array exceed a predetermined tolerance, and evaluating if a same drop dispenser is responsible when multiple error conditions are generated,. (See the specification pg 5, lines 24-27.)

Claim 22 depends from Claim 21 and specifies that the indication of the responsible drop dispenser comprises an indication of potential error in a polynucleotide containing fluid which has been preselected to be dispensed by that

drop dispenser. (See the specification pg 5, line 28.)

Claim 23 depends from Claim 1 and specifies that the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, and the method additionally comprises the control processor loading the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid; when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication; and when multiple error indications are generated, the control processor comparing a pattern of error indications with the loading pattern of the dispensers to evaluate whether one or more drop dispensers or an error in a polynucleotide containing fluid is responsible for the error indications. (See the specification pg 6, lines 7-10.)

Claim 24 depends from Claim 13 and specifies that the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and each array is to be deposited using an initial pattern of drop dispensing from the multiple dispensers, and the method additionally comprises when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication; when multiple error indications are generated, evaluating if a same drop dispenser may be responsible; and when the evaluation indicates the same drop dispenser may be responsible, altering the initial pattern such that the same drop dispenser is not used. (See the specification pg 6, lines 24-28.)

Independent Claim 25 claims an apparatus for fabricating an array of polynucleotides on a substrate, comprising a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system; an imaging system to capture an image of an actual pattern of dried spots resulting from drying of droplets deposited on the substrate; and a processor to control the deposition system to deposit the array of droplets and which, after a predetermined time has elapsed for drying of the droplets to yield the actual pattern, causes the imaging system to capture the actual pattern and compares actual pattern with the target pattern. (See the specification pg 7, lines 1-

11.)

Claim 26 depends from Claim 25 and specifies that the deposition system deposits droplets of no greater than 1000 pL. (See the specification pg 10, lines 8 and 9.)

Claim 27 depends from Claim 25 and specifies that the deposition system includes a head having multiple pulse jets each of which can dispense droplets of a fluid onto a substrate, each jet including a chamber with an orifice, and including an ejector which, when activated, causes a droplet to be ejected from the orifice. (See the specification pg 17, lines 30-32.)

Claim 28 depends from Claim 27 and specifies that the head has at least ten jets. (See the specification pg 12, lines 21-24.)

Claim 29 depends from Claim 27 and specifies that the imaging system captures a light scattering characteristic of dried spots. (See the specification pg 13, lines 23-25.)

Claim 30 depends from Claim 27 and specifies that the imaging system captures a fluorescence characteristic of dried spots. (See the specification pg 15, lines 29 and 30.)

Claim 31 depends from Claim 25 and specifies that the processor automatically: operates the deposition system to deposit multiple polynucleotide arrays; causes the imaging system to capture one or more of the images; and performs the comparison step for such arrays. (See the specification pg 18, lines 27-31.)

Claim 32 depends from Claim 25 and specifies that the apparatus additionally comprises a memory, and wherein when the results of one or more comparisons for an array exceed a predetermined tolerance, the processor stores in the memory an error indication in association with an identification of that array. (See the specification pg 19, lines 4-8.)

Claim 33 depends from Claim 32 and specifies that the error indication includes an indication of the magnitude of the error. (See the specification pg 19, lines 11 and 12.)

Claim 34 depends from Claim 25 and specifies that the apparatus additionally

comprises an audio or visual output device, and wherein the polynucleotide deposition system automatically fabricates multiple polynucleotide arrays; and when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, the processor automatically halts further operation of the deposition system and generates a visible or audible operator alert on the output device. (See the specification pg 21, lines 19-23.)

Claim 35 depends from Claim 25 and specifies that the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and wherein the processor: generates an error indication when the results of one or more comparisons for an array exceed a predetermined tolerance; and when multiple error conditions are generated, evaluates if a same drop dispenser may be responsible. (See the specification pg 22, line 30 to pg 23, line 14.)

Claim 36 depends from Claim 35 and specifies that the apparatus additionally comprises an audio or visual output device, and wherein when the evaluation indicates a same drop dispenser may be responsible the processor generates an operator alert on the output device which includes an indication of the responsible drop dispenser. (See the specification pg 21, lines 19-23.)

Claim 37 depends from Claim 25 and specifies that the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and the apparatus additionally comprises a memory, and wherein the processor: activates the drop dispensers in accordance with an initial pattern stored in the memory; generates an error indication when the results of one or more comparisons for an array exceed a predetermined tolerance; and evaluates if a same drop dispenser or an error in a polynucleotide containing fluid may be responsible by comparing the stored dispensing pattern with a pattern of error indications. (See the specification pg 22, line 30 to page 23, line 14.)

Claim 38 depends from Claim 37 and specifies that the processor alters the initial pattern in response to the result of the evaluation of the drop dispenser or polynucleotide containing fluid error. (See the specification pg 24, lines 28-30.)

Independent Claim 39 claims an apparatus for fabricating an array of polynucleotides on a substrate, comprising a polynucleotide deposition system to

deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system which may differ from the actual pattern deposited; an imaging system to capture an image of the actual pattern of spots; a processor to control the deposition system to deposit the array of droplets and which causes the imaging system to capture the actual pattern and compares the actual pattern with the target pattern; wherein the deposition system includes a head retainer to receive a fluid dispensing head, and includes a transporter to move the head retainer relative to the substrate; the imaging system includes a light receiving element mounted for movement by the transporter. (See the specification pg 11, lines 15-29.)

Claim 40 depends from Claim 39 and specifies that the light receiving element includes a light sensor. (See the specification pg 14, lines 3 and 4.)

Claim 41 depends from Claim 1 and specifies that the actual pattern is compared with the target pattern for spot location, dimension or presence, the method additionally comprising generating a signal indicative of the result of the comparison. (See the specification pg 18, lines 30 and 31.)

Claim 42 depends from Claim 25 and specifies that the processor compares the actual pattern with the target pattern for spot location, dimension or presence, and additionally generates a signal indicative of the result of the comparison. (See the specification pg 18, lines 27-30.)

Claim 43 depends from Claim 1 and specifies that the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, and the method additionally comprises the control processor: loading the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid; performing the comparisons of the actual and target patterns and, when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication; and when an error indication is generated, operating the drop dispensers to correct for the error. (See the specification pg 7, lines 17-21.)

Claim 44 depends from Claim 43 and specifies that when the error indication

is caused by incorrect drop dispenser operation, the processor uses another drop dispenser to correctly deposit a drop on the same array. (See the specification pg 5, lines 22 and 23.)

Claim 45 depends from Claim 44 and specifies that the drop dispensers are pulse jets. (See the specification pg 5, line 23.)

Independent Claim 46 claims an apparatus wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, wherein the control processor: loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid; performs the comparisons of the actual and target patterns and, when the results of one or more comparisons for an array exceed a predetermined tolerance, generates an error indication; and when an error indication is generated, operating the drop dispensers to correct for the error. (See the specification pg 22, line 30 to pg 23, line 14.)

Claim 47 depends from Claim 46 and specifies that when the error indication is caused by incorrect drop dispenser operation, the processor uses another drop dispenser to correctly deposit a drop on the same array. (See the specification pg 23, lines 14-20.)

Claim 48 depends from Claim 37 and specifies that the drop dispensers are pulse jets. (See the specification pg 23, lines 19 and 20.)

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 1-18 and 20-48 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Baldeschwieler et al. (US Patent No. 6,015,880) in view of Weber et al. (US Patent No. 4,328,504).

Claims 1-18 and 20-48 stand rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Graves et al., Anal. Chem. 1998, 70:5085-5092 or in the alternative, under 35 U.S.C. § 103(a) as allegedly being obvious over Graves et al.

ARGUMENTS

In maintaining the rejection under § 103 of Baldeschwieler et al. in view of Weber et al., the Examiner has employed the Weber et al. patent, which is clearly drawn to subject matter that is non-analogous to that of the primary document, Baldeschwieler et al.

In the following sections, the Appellants will demonstrate why the Examiner's *prima facie* case of obviousness is deficient. Specifically, it is respectfully submitted that the Examiner's *prima facie* case of obviousness is deficient because the Examiner has combined improperly two patents from non-analogous arts. In addition, the Appellants were the first to identify and solve a specific problem in the manufacturing of biopolymer arrays, a fact which is a basis for unobviousness over the cited documents. Below are the contentions of the Appellants with respect to the ground of rejection.

In maintaining the rejection under § 102(a) over Graves et al., the Examiner has incorrectly concluded that a target array pattern determined by a processor in communication with the deposition system is inherently disclosed in Graves et al. In maintaining the rejection under § 103(a) over Graves et al., the Examiner has employed hindsight to reach a conclusion that one would have been motivated to produce arrays in accordance with a target array pattern that is determined by a processor in communication with the deposition system.

In the following sections, the Appellants will demonstrate why the Examiner's anticipation rejection and *prima facie* case of obviousness are deficient. Specifically, it is respectfully submitted that the anticipation rejection is deficient because all of the claim elements are not identically disclosed in Graves et al., and the Examiner has not established inherency. The obviousness rejection is deficient because all of the claim elements are neither taught nor suggested by Graves et al., and there would have been no motivation to arrive at Appellants' invention.

Below are the contentions of the Appellants with respect to the grounds of rejection.

The claims will be argued as nine groups, namely

Group I: Claims 1-9, 12-18, 20-22, and 41
Group II: Claims 25-38, and 42
Group III: Claim 10
Group IV: Claim 11
Group V: Claim 20
Group VI: Claim 23 and 43-45
Group VII: Claim 24
Group VIII: Claims 39 and 40
Group IX: Claims 46-48

I. Claims 1-18 and 20-48 are not obvious under 35 U.S.C. § 103(a) over Baldeschwieler et al. (US Patent No. 6,015,880) in view of Weber et al. (US Patent No. 4,328,504).

With respect to rejections made under 35 U.S.C. § 103, MPEP § 2142 states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Group I: Claims 1-9, 12-18, 20-22, and 41

The claims of this group recite a method of fabricating an array of polynucleotides on a substrate.

The Examiner's rationale for making this rejection is that Baldeschwieler et al. discloses a method for fabricating biopolymer arrays, which method employs an ink jet device for reagent deposition. Baldeschwieler et al., however, is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target pattern.

Weber et al. was cited by the Examiner in an effort to remedy the deficiency of Baldeschwieler et al. However, Weber et al. is drawn to correction of printing errors when printing ink is deposited onto paper, and not to correction of errors associated with the deposition of aqueous biopolymers or precursors thereof onto a surface in order to produce an array that is useful in biotechnological applications. Furthermore, the Weber et al. process does not include a comparison of dried spots, as in the present claims. As such, Weber et al. does not remedy the deficiency of Baldeschwieler et al.

In addition, one would not have expected the problems faced by Weber et al. to be reasonably pertinent either to those faced by Baldeschwieler et al. or to those faced by the Appellants. The technical field of Weber et al. is from an art that is non-analogous to the art of Baldeschwieler et al. Baldeschwieler et al. does not use printing ink whereas Weber et al. does, and Baldeschwieler et al. is not printing onto paper whereas Weber et al. is.

The Examiner has asserted only that both Baldeschwieler et al. and Weber et al. employ ink jet devices, which allegedly makes the two documents analogous. This assertion by the Examiner is inconsistent with the criteria for analogous art set forth in MPEP § 2141.01(a), namely:

> 'In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was

> concerned.' *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). See also *In re Deminski*, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986); *In re Clay*, 966 F.2d 656, 659, 23 USPQ2d 1058, 1060-61 (Fed. Cir. 1992) ('A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem.'); *Wang Laboratories Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767 (Fed. Cir. 1993); and *State Contracting & Eng'g Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 1069, 68 USPQ2d 1481, 1490 (Fed. Cir. 2003) (where the general scope of a reference is outside the pertinent field of endeavor, the reference may be considered analogous art if subject matter disclosed therein is relevant to the particular problem with which the inventor is involved).

Conventional ink jet printing of printing ink onto paper would not logically commend itself to an inventor in the biopolymer array art in considering problems with making arrays via deposition of biopolymers because printing ink onto paper is so completely different from depositing chemical reagents onto a substrate to make microarrays. Differences between the two applications are multitude and include different types of materials employed. For example, conventional printing employs ink and the methods of claimed invention employ nucleic acid monomer reagent. In addition, the protocols are different. For example, use of conventional ink is a single pass process. In contrast, the claims are directed to fabrication of biopolymer arrays, where a plurality of passes, and various conditions, are required to build up the nucleic acid polymers. Differences further extend to the end products, where the end product in conventional ink jet printing is a printed page and the end product of the present application is a nucleic acid array. Furthermore, conventional ink jet printing is in a completely different field of endeavor from the present application, where ink jet printing is in the field of publishing and the claims of the present application are directed to fabrication of nucleic acid arrays for use in biotechnological assay applications.

Nor would the particular problems with conventional ink printing onto paper be reasonably pertinent to making biopolymer arrays. As such, Weber et al is not properly combinable with Baldeschwieler et al. Accordingly, a *prima facie* case of obviousness has not been established. Appellants respectfully request withdrawal of this rejection.

In addition to the fact that the cited documents are not combinable for the reasons set forth above, Appellants emphasize that they were the first to recognize a specific problem in the fabrication of biopolymer arrays, and that they then succeeded in solving that problem. Specifically, the present invention is directed to the problem in which positive features during an array assay nonetheless give rise to a weak signal that may be difficult to distinguish from background, particularly at the feature border. This problem can become exaggerated when the array pattern of a given array is different from the target array pattern according to which the array was fabricated due to errors arising during the manufacture process.

As such, it is desirable during the manufacture of an array to ensure that any discrepancy between an actual array pattern and the target array pattern according to which it was fabricated be kept at a minimum. Such is desirable so that, during use, one can know precisely where features of the array are located. These problems were not appreciated by Baldeschwieler et al. or Weber et al.

Recognition by Appellants of a problem in the art and solving that problem are a basis for a determination of the unobviousness of Appellants' claimed invention. "[Where] there is no evidence of record that a person of ordinary skill in the art at the time of [an applicant's] invention would have expected [a problem] ... to exist at all, it is not proper to conclude that [an invention] ... which solves this problem ... would have been obvious to that hypothetical person of ordinary skill in the art." *In re Peehs*, 612 F.2d 1287, 1290, 204 USPQ 835 (CCPA 1980) (citing *In re Nomiya*, 509 F.2d 566, 572, 184 USPQ 607, 612-13 (CCPA 1975))(emphasis added).

The Examiner has not established that the problem in the biopolymer array art that was recognized and solved by the Appellants was known or expected *in the biopolymer array art*. It is her burden to do so, but in the Advisory Action mailed March 15, 2006, she has required an affidavit or declaration from the Appellants. The quotation from *Peehs* above implies that the evidence of record must be

supplied by the Examiner, for it is the Examiner who makes the conclusion of obviousness. Absent that evidence, a conclusion of obviousness by the Examiner is improper.

Moreover, the secondary considerations listed by the Examiner in the Advisory Action that require an affidavit or declaration do not include recognition and solution of a problem in the art. Appellants' specification, for example at the paragraph bridging pages 2 and 3, is a disclosure of Appellants' recognition of the problem; the remainder of the specification discloses the solution. Appellants have already signed a declaration that they have reviewed and understood the contents of their specification. A further declaration by Appellants is therefore unnecessary.

The Appellants also reiterate that without an appreciation of the problem solved by the present invention, there would have been no motivation to combine the teachings of Baldeschwieler et al. and Weber et al. to arrive at the claimed invention because there would have been no motivation to look to non-analogous art to solve an unrecognized problem in the biopolymer array art. Without knowledge of the problem, there would have been no need to combine the documents, the expense of making the combination would be high, and there would have been no expected benefit to making the combination.

Furthermore, one would not have been motivated to go the extra step of correcting for errors so as to reduce discrepancies between the actual and target array pattern, because one would not have appreciated that such discrepancies would occur or further that such discrepancies, if present, would have any effect on the usability of the array. In fact, one of skill in the art would not have been motivated to modify Baldeschwieler et al. because any such modification would have added to the expense of the process without yielding any benefit.

Therefore, for the additional reason that there would have been no motivation to combine the teachings of Baldeschwieler et al. and Weber et al., a *prima facie* case of obviousness has not been established. Appellants respectfully request

withdrawal of this rejection.

Group II: Claims 25-38 and 42

The claims of this group recite an apparatus for fabricating an array of polynucleotides on a substrate, comprising an imaging system to capture an image of an actual pattern of dried spots.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches or suggests an apparatus comprising an imaging system to capture an image of an actual pattern of dried spots.

As described in Appellants' specification, an imaging system can include any system which can provide spatial information as to the location of dried drops. However, Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process (via an imaging system or any other system) so as to reduce discrepancies between a dried actual pattern and a target pattern, and Weber et al. does not include a comparison of dried spots, as in the present claims.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claim of this group, Appellants respectfully request withdrawal of this rejection.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group III: Claim 10

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a light scattering characteristic of dried spots.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches or suggests a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a light scattering characteristic of dried spots.

As described in Appellants' specification, an image capturing system can include any system which can provide spatial information as to the location of dried drops. However, Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process (via an image capturing system or any other system) so as to reduce discrepancies between a dried actual pattern and a target pattern, and Weber et al. does not include a comparison of dried spots, much less a light scattering characteristic of dried spots, as in the present claim.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group IV: Claim 11

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a fluorescence characteristic of dried spots.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches

or suggests a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a fluorescence characteristic of dried spots.

As described in Appellants' specification, an image capturing system can include any system which can provide spatial information as to the location of dried drops. However, Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process (via an image capturing system or any other system) so as to reduce discrepancies between a dried actual pattern and a target pattern, and Weber et al. does not include a comparison of dried spots, much less a fluorescence characteristic of a dried spot, as in the present claim.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group V: Claim 20

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, wherein the further operation is halted automatically.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches or suggests a method for fabricating an array of polynucleotides on a substrate, wherein the further operation is halted automatically.

As described in Appellants' specification, when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, further operation of the deposition system is halted automatically. However, Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual

pattern and a target pattern, and Weber et al. does not include a comparison of dried spots or automatic halting of operation, as in the present claim.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group VI: Claims 23 and 43-45

The claims of this group recite a method for fabricating an array of polynucleotides on a substrate, wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches or suggests a method for fabricating an array of polynucleotides on a substrate, wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

As described in Appellants' specification, in the case where the dispensing head has multiple drop dispensers and the deposition system includes a control processor, the control processor may direct loading of the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid. However, Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target pattern, and Weber et al. does not include a comparison of dried spots or loading of dispensers under the direction of a control processor, as in the present claims.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group VII: Claim 24

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, comprising altering the initial pattern such that the some drop dispenser is not used.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches or suggests a method for fabricating an array of polynucleotides on a substrate, comprising altering the initial pattern such that the some drop dispenser is not used.

As described in Appellants' specification, when an evaluation of multiple error indications indicates that a same drop dispenser in a multiple drop dispenser head may be responsible (that is, it is suspect), the method may include altering an initial deposition pattern from the head (such as may have been formulated or accessed by a control processor) such that the suspect drop dispenser is not used. However, Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target pattern, and Weber et al. does not include a comparison of dried spots or altering a deposition pattern such that a suspect drop dispenser is not used, as in the present claim.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group VIII: Claims 39 and 40

The claims of this group recite an apparatus for fabricating an array of polynucleotides on a substrate, comprising an imaging system that includes a light receiving element mounted for movement by the transporter.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches or suggests an apparatus comprising an imaging system that includes a light receiving element mounted for movement by the transporter.

Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process (via an imaging system or any other system), and Weber et al. does not include an imaging system that includes a light receiving element mounted for movement by the transporter, as in the present claims.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group IX: Claims 46-48

The claims of this group recite an apparatus for fabricating an array of polynucleotides on a substrate, wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that neither Baldeschwieler et al. nor Weber et al. teaches or suggests an apparatus wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

As described in Appellants' specification, in the case where the dispensing head has multiple drop dispensers and the deposition system includes a control processor, the control processor may direct loading of the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid. However, Baldeschwieler et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target pattern, and the apparatus of Weber et al. does not provide for loading of dispensers under the direction of a control processor, as in the present claims.

Accordingly, because the combination of the teachings of Baldeschwieler et al. and Weber et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

II. Claims 1-18 and 20-48 are not unpatentable under 35 U.S.C. 102(a) over Graves et al., Anal. Chem. 1998, 70:5085-5092 or in the alternative, under 35 U.S.C. § 103(a) over Graves et al.

Group I: Claims 1-9, 12-18, 20-22, and 41

The claims of this group recite a method of fabricating an array of polynucleotides on a substrate.

The Examiner's rationale for anticipation is that a target array pattern is inherent in Graves et al. by virtue of the reproducible arrays produced by Graves et al. Such an assertion is conclusory, and is unsupported by factual and technical grounds establishing that the inherent feature must flow as a necessary conclusion.

In rejecting claims based in inherency, the Patent Office must provide objection evidence or cogent technical reasoning tending to show inherency. (See MPEP § 2112). In the present case, the allegation of inherency is merely conclusory

and the Examiner has provided no evidence or reasoning to support the Examiner's position. The fact that a certain result or characteristic may occur or be present i the prior art is not sufficient to establish inherency of that result or characteristic, *In re Rijckaert*, 28 U.S. P.Q. 2d 1955, 1957 (Fed. Cir. 1993). Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient, *In re Robertson,* 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999).

In addition, Graves et al. fails to teach or suggest all the elements of all the rejected claims. For example, forwarding the array and medium to a remote user (Claim 18); the fluid dispensing head with multiple drop dispensers (Claim 21); and the control processor's comparing and evaluating function when multiple error indications are generated (Claim 23) are included in the rejection with no apparent rationale or justification. Accordingly, because Graves et al. does not teach every element of the presently claimed invention, there is no anticipation or *prima facie* obviousness.

The Examiner's rationale for obviousness is that it would have been obvious to use the method of Graves et al. to produce arrays in accordance with a defined pattern.

Fundamentally, Graves et al. is not concerned with fabricating arrays according to a target array pattern. The Examiner acknowledges this fact at the penultimate line of page 4 of the Final Office Action. Graves et al. is concerned primarily with reproducibility of deposition. Comparison for reproducibility of a first printed array with subsequent printed arrays, as in Graves et al., is not the same as Appellants' claims, which recite that a polynucleotide deposition system is operated to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system.

Graves et al. does not teach or suggest a polynucleotide deposition system operated to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system. The software of Graves et al. permits the user to specify movement in two directions. Graves et al. at page 5086, first column. This is very different from a target array pattern that is determined by a processor in communication with the deposition system, as in Appellants' present claims. For the additional reason that there would have been no motivation to employ such a target array pattern absent the guidance provided by the Appellants' disclosure, there is no prima facie obviousness.

In the Advisory Action, the Examiner asserted that the spacing of deposition needles in Graves et al. is a target pattern as in Appellants' claims. However, this is again very different from a target array pattern that is determined by a processor in communication with the deposition system, as in Appellants' present claims.

Appellants respectfully request withdrawal of this rejection.

Group II: Claims 25-38 and 42

The claims of this group recite an apparatus for fabricating an array of polynucleotides on a substrate, comprising an imaging system to capture an image of an actual pattern of dried spots.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest an apparatus comprising an imaging system to capture an image of an actual pattern of dried spots.

As described in Appellants' specification, an imaging system can include any system which can provide spatial information as to the location of dried drops.

However, Graves et al. is deficient for not disclosing the correction of errors in the deposition process via an imaging system so as to reduce discrepancies between a dried actual pattern and a target pattern

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group III: Claim 10

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a light scattering characteristic of dried spots.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a light scattering characteristic of dried spots.

As described in Appellants' specification, an imaging system can include any system which can provide spatial information as to the location of dried drops. However, Graves et al. is deficient for not disclosing the correction of errors in the deposition process via an imaging system comprising imaging a light scattering characteristic of dried spots so as to reduce discrepancies between a dried actual pattern and a target pattern

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group IV: Claim 11

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a fluorescence characteristic of dried spots.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest a method for fabricating an array of polynucleotides on a substrate, wherein the image capture comprises imaging a fluorescence characteristic of dried spots.

As described in Appellants' specification, an imaging system can include any system which can provide spatial information as to the location of dried drops. However, Graves et al. is deficient for not disclosing the correction of errors in the deposition process via an imaging system comprising imaging a fluorescence characteristic of dried spots so as to reduce discrepancies between a dried actual pattern and a target pattern

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group V: *Claim 20*

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, wherein the further operation is halted automatically.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest a method for fabricating an array of polynucleotides on a substrate, wherein the further operation is halted automatically.

As described in Appellants' specification, when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, further operation of the deposition system is halted automatically. However, Graves et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target pattern, and Graves et al. does not include automatic halting of operation, as in the present claim.

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group VI: Claims 23 and 43-45

The claims of this group recite a method for fabricating an array of polynucleotides on a substrate, wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest a method for fabricating an array of polynucleotides on a substrate, wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

As described in Appellants' specification, in the case where the dispensing head has multiple drop dispensers and the deposition system includes a control processor, the control processor may direct loading of the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid. However, Graves et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target

pattern, and Graves et al. does not include loading of dispensers under the direction of a control processor, as in the present claims.

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group VII: Claim 24

The claim of this group recites a method for fabricating an array of polynucleotides on a substrate, comprising altering the initial pattern such that the some drop dispenser is not used.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest a method for fabricating an array of polynucleotides on a substrate, comprising altering the initial pattern such that the some drop dispenser is not used.

As described in Appellants' specification, when an evaluation of multiple error indications indicates that a same drop dispenser in a multiple drop dispenser head may be responsible (that is, it is suspect), the method may include altering an initial deposition pattern from the head (such as may have been formulated or accessed by a control processor) such that the suspect drop dispenser is not used. However, Graves et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target pattern, and Graves et al. does not include altering a deposition pattern such that a suspect drop dispenser is not used, as in the present claim.

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group VIII: Claims 39 and 40

The claims of this group recite an apparatus for fabricating an array of polynucleotides on a substrate, comprising an imaging system that includes a light receiving element mounted for movement by the transporter.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest an apparatus comprising an imaging system that includes a light receiving element mounted for movement by the transporter.

Graves et al. is deficient for not disclosing the correction of errors in the deposition process via an imaging system so as to reduce discrepancies between a dried actual pattern and a target pattern, and Graves et al. does not include an imaging system that includes a light receiving element mounted for movement by the transporter, as in the present claims.

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

Group IX: Claims 46-48

The claims of this group recite an apparatus for fabricating an array of polynucleotides on a substrate, wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

In addition to the arguments detailed above for the Claims of Group I, Appellants further submit that Graves et al. does not teach or suggest an apparatus

wherein the control processor loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid.

As described in Appellants' specification, in the case where the dispensing head has multiple drop dispensers and the deposition system includes a control processor, the control processor may direct loading of the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid. However, Graves et al. is deficient for not disclosing the correction of errors in the deposition process so as to reduce discrepancies between a dried actual pattern and a target pattern, and the system of Graves et al. does not provide for loading of dispensers under the direction of a control processor, as in the present claims.

Accordingly, because Graves et al. fails to teach or suggest each and every element of the claims of this group, Appellants respectfully request withdrawal of this rejection.

SUMMARY

Claims 1-18 and 20-48 are not unpatentable under 35 U.S.C. § 103(a) over Baldeschwieler et al. (US Patent No. 6,015,880) in view of Weber et al. (US Patent No. 4,328,504) because Baldeschwieler et al. does not disclose the correction of errors in a process for the deposition of aqueous biopolymers or precursors thereof so as to reduce discrepancies between an actual and a target pattern, and Weber et al. does not remedy the deficiency of Baldeschwieler et al.

Claims 1-18 and 20-48 are not unpatentable under 35 U.S.C. § 102(a) or § 103(a) over Graves et al. because the Examiner has not established inherency, all the elements of Appellants' claims are not identically disclosed, taught, or suggested by Graves et al., and there would have been no motivation to employ a target array pattern that is determined by a processor in communication with the deposition system absent the guidance provided by the Appellants' disclosure.

RELIEF REQUESTED

The Appellants respectfully requests that the rejection of Claims 1-18 and 20-48 under 35 U.S.C. § 103(a) be reversed, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,

Date: June 20, 2006 By: _____

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Claims Appendix

1. A method of fabricating an array of polynucleotides on a substrate, comprising:

(a) operating a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system;

(b) allowing a sufficient time to pass such that droplets deposited by the system will have dried to yield an actual pattern of dried spots; and

(c) observing the actual pattern; and

(d) comparing the actual pattern with the target pattern.

2. A method according to claim 1 wherein the actual pattern is observed by capturing an image of the actual pattern.

3. A method according to claim 1 wherein the system deposits fluid droplets at least some of which contain respective different polynucleotides.

4. A method according to claim 1 wherein the one or more polynucleotide containing fluids each comprise a solution of a polynucleotide and a sufficient amount of salt to enhance polynucleotide imaging.

5. A method according to claim 1 wherein the polynucleotides are DNA of at least six nucleotides in length.

6. A method according to claim 5 wherein the DNA is cDNA.

7. A method according to claim 5 wherein the DNA is single stranded.

8. A method according to claim 1 wherein the comparison includes a

comparison of dried actual spot locations or dimensions with target locations or dimensions.

9. A method according to claim 1 wherein the comparison includes a comparison of the presence or absence of dried spots at target locations.

10. A method according to claim 1 wherein the image capture comprises imaging a light scattering characteristic of dried spots.

11. A method according to claim 1 wherein the image capture comprises imaging a fluorescence characteristic of dried spots.

12. A method according to claim 1 additionally comprising generating a signal indicative of the result of the comparison.

13. A method according to claim 1 wherein the deposition system is operated to fabricate multiple polynucleotide arrays on a same substrate.

14. A method according to claim 1 additionally comprising:

when the results of one or more comparisons for an array exceed a predetermined tolerance, storing an error indication in association with that array.

15. A method according to claim 14 wherein the deposition system is operated to fabricate multiple polynucleotide arrays, the method additionally comprising rejecting the array associated with a stored error indication.

16. A method according to claim 14 wherein the error indication is stored in a memory, the method additionally comprising writing on a medium an identification for the array associated with an error indication; physically associating that medium with the array; and storing the identification in the memory.

17. A method according to claim 16 wherein the error indication includes an indication of the magnitude of the error.

18. A method of fabricating an array of polynucleotides on a substrate, comprising:

(a) operating a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system which may differ from the actual pattern deposited;

(b) capturing an image of the actual pattern;

(c) comparing the actual pattern with the target pattern;

(d) when the results of one or more comparisons for an array identify the presence of a first level error, generating a first level error indication associated with the array;

(e) writing the error indication or an identification of the error indication, on a medium; physically associating the medium with the array; and, when an identification of the error indication is written on the medium, storing the identification in a memory in association with the error indication; and

(f) forwarding the array and medium to a remote user.

20. A method according to claim 1 wherein the polynucleotide deposition system automatically fabricates multiple polynucleotide arrays, the method additionally comprising, when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, automatically halting further operation of the deposition system and generating a visible or audible operator alert.

21. A method according to claim 1 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, the method additionally comprising:

when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication;

when multiple error conditions are generated, evaluating if a same drop dispenser is responsible;

and wherein, when the evaluation indicates the same drop dispenser is responsible, generating a visible or audible operator alert which includes an indication of the responsible drop dispenser.

22. A method according to claim 21 wherein the indication of the responsible drop dispenser comprises an indication of potential error in a polynucleotide containing fluid which has been preselected to be dispensed by that drop dispenser.

23. A method according to claim 1 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, the method additionally comprising:
the control processor loading the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid;
when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication;
when multiple error indications are generated, the control processor comparing a pattern of error indications with the loading pattern of the dispensers to evaluate whether one or more drop dispensers or an error in a polynucleotide containing fluid is responsible for the error indications.

24. A method according to claim 13 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and each array is to be deposited using an initial pattern of drop dispensing from the multiple dispensers, the method additionally comprising:
when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication;
when multiple error indications are generated, evaluating if a same drop dispenser

may be responsible; and
when the evaluation indicates the same drop dispenser may be responsible, altering the initial pattern such that the same drop dispenser is not used.

25. An apparatus for fabricating an array of polynucleotides on a substrate, comprising:
(a) a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system;
(b) an imaging system to capture an image of an actual pattern of dried spots resulting from drying of droplets deposited on the substrate;
(c) a processor to control the deposition system to deposit the array of droplets and which, after a predetermined time has elapsed for drying of the droplets to yield the actual pattern, causes the imaging system to capture the actual pattern and compares actual pattern with the target pattern.

26. An apparatus according to claim 25 wherein the deposition system deposits droplets of no greater than 1000 pL.

27. An apparatus according to claim 25 wherein the deposition system includes a head having multiple pulse jets each of which can dispense droplets of a fluid onto a substrate, each jet including a chamber with an orifice, and including an ejector which, when activated, causes a droplet to be ejected from the orifice.

28. An apparatus according to claim 27 wherein the head has at least ten jets.

29. An apparatus according to claim 27 wherein the imaging system captures a light scattering characteristic of dried spots.

30. An apparatus according to claim 27 wherein the imaging system captures a fluorescence characteristic of dried spots.

31. An apparatus according to claim 25 wherein the processor automatically: operates the deposition system to deposit multiple polynucleotide arrays; causes the imaging system to capture one or more of the images; and performs the comparison step for such arrays.

32. An apparatus according to claim 25 additionally comprising a memory, and wherein when the results of one or more comparisons for an array exceed a predetermined tolerance, the processor stores in the memory an error indication in association with an identification of that array.

33. An apparatus according to claim 32 wherein the error indication includes an indication of the magnitude of the error.

34. An apparatus according to claim 25 additionally comprising an audio or visual output device, and wherein:
the polynucleotide deposition system automatically fabricates multiple polynucleotide arrays; and
when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, the processor automatically halts further operation of the deposition system and generates a visible or audible operator alert on the output device.

35. An apparatus according to claim 25 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and wherein the processor:
generates an error indication when the results of one or more comparisons for an array exceed a predetermined tolerance; and
when multiple error conditions are generated, evaluates if a same drop dispenser may be responsible

36. An apparatus according to claim 35 additionally comprising an audio or visual output device, and wherein when the evaluation indicates a same drop dispenser may be responsible the processor generates an operator alert on the output device which includes an indication of the responsible drop dispenser.

37. An apparatus according to claim 25 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, the apparatus additionally comprising a memory, and wherein the processor:

activates the drop dispensers in accordance with an initial pattern stored in the memory;

generates an error indication when the results of one or more comparisons for an array exceed a predetermined tolerance; and

evaluates if a same drop dispenser or an error in a polynucleotide containing fluid may be responsible by comparing the stored dispensing pattern with a pattern of error indications.

38. An apparatus according to claim 37 wherein the processor alters the initial pattern in response to the result of the evaluation of the drop dispenser or polynucleotide containing fluid error.

39. An apparatus for fabricating an array of polynucleotides on a substrate, comprising:

(a) a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system which may differ from the actual pattern deposited;

(b) an imaging system to capture an image of the actual pattern of spots;

(c) a processor to control the deposition system to deposit the array of droplets and which causes the imaging system to capture the actual pattern and compares the actual pattern with the target pattern;

wherein:

the deposition system includes a head retainer to receive a fluid dispensing head, and includes a transporter to move the head retainer relative to the substrate;

the imaging system includes a light receiving element mounted for movement by the transporter.

40. An apparatus according to claim 39 wherein the light receiving element includes a light sensor.

41. A method according to claim 1 wherein the actual pattern is compared with the target pattern for spot location, dimension or presence, the method additionally comprising generating a signal indicative of the result of the comparison.

42. An apparatus according to claim 25 wherein the processor compares the actual pattern with the target pattern for spot location, dimension or presence, and additionally generates a signal indicative of the result of the comparison.

43. A method according to claim 1 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, the method additionally comprising the control processor:
loading the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid;
performing the comparisons of the actual and target patterns and, when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication; and
when an error indication is generated, operating the drop dispensers to correct for the error.

44. A method according to claim 43 wherein when the error indication is caused by incorrect drop dispenser operation, the processor uses another drop dispenser to correctly deposit a drop on the same array.

45. A method according to claim 44 wherein the drop dispensers are pulse jets.

46. An apparatus wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, wherein the control processor:
loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid;
performs the comparisons of the actual and target patterns and, when the results of one or more comparisons for an array exceed a predetermined tolerance, generates an error indication; and
when an error indication is generated, operating the drop dispensers to correct for the error.

47. An apparatus according to claim 46 wherein when the error indication is caused by incorrect drop dispenser operation, the processor uses another drop dispenser to correctly deposit a drop on the same array.

48. An apparatus according to claim 47 wherein the drop dispensers are pulse jets.

EVIDENCE APPENDIX

No evidence submitted under 37 CFR §§ 1.130, 1.131 or 1.132 has been relied upon by Appellants in this Appeal.

RELATED PROCEEDINGS APPENDIX

There are no decisions rendered by a court or the Board which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.